

R E M A R K S

This is in response to the Office Action that was filed on August 23, 2002. Claims 1 and 2 are amended to incorporate features recited in original claims 3 and 4. Claims 1, 2, and 5 are also amended to incorporate a feature that is shown in Figures 1 and 2 of the drawings and disclosed, *e.g.*, in the paragraph bridging pages 12-13 of the specification (“Fig. 1 shows an example using the linear union in which the inner diameter of a part (3) of the solvent inlet tube (1) and outlet tube (2) is larger than the other portion, and Fig. 2 shows an example in which a frit (4) is inserted into the part (3) having a larger inner diameter than the other portion in the diffusion promoting device.”). Claims 6 and 7 are not amended. Only minor formal amendments are made to claims 8-13. No new matter is introduced by this Amendment. Claims 1, 2, and 5-13 are in the case.

FORMAL REJECTIONS. Claims 1-14 were rejected under the second paragraph of 35 U.S.C. 112. The present amendments address and obviate all of the grounds put forth by the Examiner in connection with this rejection, except that Applicants respectfully traverse the Examiner’s indication that the metes and bound of “low flow velocity” cannot be determined. Applicants respectfully submit that the language “low flow velocity gradient high performance liquid chromatographic apparatus” is well known to those skilled in the art, as noted in the paragraph bridging pages 2-3 of the specification, and that Applicants have in any case provided a detailed explanation of what that language means in the context of the present invention, in the full first paragraph on page 9 of the specification. Accordingly, Applicants respectfully submit that the claims in their present form satisfy the requirements of the statute.

THE PRESENT INVENTION. The present invention distinguishes over the prior art of record by placing the diffusion promoting device just before the separation column. This permits a sample being analyzed to be retained uniformly at the beginning end of the separation column. The sample is diffused or dispersed uniformly by way of the diffusion promoting device before the separation column and it can be treated uniformly in the separation column. A sufficient concentration of the target compound in an eluent can thus be obtained to effect a gradient elution. "The present invention provides a diffusion promoting device provided just before a separation column and having a function of improving detection sensitivity, in a low flow velocity high performance liquid chromatographic apparatus. The present invention also provides a method for improving detection sensitivity of a target component for use in a low flow velocity gradient high performance liquid chromatographic apparatus, wherein a diffusion promoting device is provide just before a separation column." Specification, page 6, 2<sup>nd</sup> and 3<sup>rd</sup> full paragraphs.

THE PRIOR ART. Claims 1-8 were rejected under 35 U.S.C. 102(b) as being anticipated by, or in the alternative, under 35 U.S.C. 103(a) as being unpatentable over, Koch. Claims 1, 2, and 9-14 were rejected under 35 U.S.C. 102(b) as being anticipated by, or in the alternative, under 35 U.S.C. 103(a) as being unpatentable over, Asakawa. Claims 12-14 were rejected under 35 U.S.C. 103(a) as being unpatentable over Asakawa in view of Snyder. Claim 14 was rejected under 35 U.S.C. 103(a) as being unpatentable over either Koch or Asakawa, each in view of Snyder. This last rejection has been rendered moot by the cancellation of claim 14. Applicants respectfully traverse the remaining prior art rejections, to the extent that they might be applied to the claims herein in their present form. The Koch reference shows a mixing chamber that has a structure, as shown in Figures 2 and 3, which appears to be similar to

certain embodiments of the present invention. Asakawa discloses a high performance liquid chromatographic (HPLC) apparatus. Snyder relates to analyzing trace amounts of samples via liquid chromatography. Not one of these references, however, teaches or suggests displacement of the mixing device just before the separation column, and accordingly none of these references would enable a person of ordinary skill in the art to obtain the advantages provided by the present invention. Accordingly, it is respectfully submitted that the Examiner has failed to establish a *prima facie* case of obviousness with respect to the present invention as it is defined by the claims in their present form.

Conclusion

If the Examiner has any questions concerning this application, he is requested to contact Richard Gallagher, Reg. No. 28,781, at (703) 205-8000 in the Washington, D.C. area.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachment: Version with Markings to Show Changes Made

***Marked up text showing changes:***

**IN THE SPECIFICATION:**

The 2<sup>nd</sup> full paragraph on page 6 has been amended as follows:

The present invention provides a diffusion promoting device provided just before a separation column and having a function of [for] improving detection sensitivity, in a low flow velocity high performance liquid chromatographic apparatus.

The 3<sup>rd</sup> full paragraph on page 6 has been amended as follows:

The present invention also provides a method for improving detection sensitivity of a target component for use in a low flow velocity gradient high performance liquid chromatographic apparatus, wherein a diffusion promoting device is provided [provide] just before a separation column.

The paragraph bridging pages 12-13 of the specification has been amended as follows:

Fig. 1 shows an example using the [liner] linear union in which the inner diameter of a part (3) of the solvent inlet tube (1) and outlet tube (2) is larger than the other portion, and Fig. 2 shows an example in which a frit (4) is inserted into the part (3) having a larger inner diameter than the other portion in the diffusion promoting device.

**IN THE CLAIMS:**

Cancel claims 3, 4, and 14, without prejudice.

The claims have been amended as follows:

1. (amended) [In a low flow velocity gradient high performance liquid chromatographic apparatus, a] A diffusion promoting device provided just before a separation column and having a function for improving detection sensitivity, wherein said device comprises a solvent inlet tube and a solvent outlet tube and wherein said device includes at least one feature selected from the group consisting of (i) having a solvent inlet tube and a solvent outlet tube with different inner diameters, (ii) having a solvent outlet tube connected to a solvent inlet tube at an acute angle, a right angle, or an obtuse angle, and (iii) having a solvent outlet tube connected to a solvent inlet tube by a connecting part having a diameter that is larger than the diameters of the diameters of the solvent inlet and outlet tubes.

2. (amended) A method for improving a detection sensitivity of a target component, which comprises providing the diffusion promoting device just before a separation column in a low flow velocity gradient high performance liquid chromatographic apparatus, wherein said diffusion promoting device comprises a solvent inlet tube and a solvent outlet tube and wherein said device includes at least one feature selected from the group consisting of (i) having a solvent inlet tube and a solvent outlet tube with different inner diameters, (ii) having a solvent outlet tube connected to a solvent inlet tube at an acute angle, a right angle, or an obtuse angle, and (iii) having a solvent outlet tube connected to a solvent inlet tube by a connecting part having a diameter that is larger than the diameters of the diameters of the solvent inlet and outlet tubes.

5. (amended) The diffusion promoting device according to Claim 1 [or 3], wherein a frit is inserted [in the solvent inlet tube and/or outlet tube] into at least one of the solvent inlet tube, the solvent outlet tube, and a position between the solvent inlet tube and the solvent outlet tube.

8. (amended) A low flow velocity high performance liquid chromatographic apparatus comprising the diffusion promoting device according to Claim 1 [or 3] at just before the separation column.

9. (amended) A low flow velocity high performance liquid chromatographic apparatus in which the diffusion promoting device according to Claim 1 [or 3] is connected between the component concentration column and the separation column.

10. (twice amended) A low flow velocity high performance liquid chromatographic apparatus in which a solvent pump (P1), an injector (I), a switching valve (V) are connected in this order in one line; and a solvent pump (P2), a switching valve (V), the diffusion promoting device (DU) according to Claim 1, a separation column (C) and a detector (D) are connected in another line[ as shown in Fig. 8].

11. (twice amended) A low flow velocity high performance liquid chromatographic apparatus in which a solvent pump (P1), a switching valve (V), a solvent mixer (MC) and a switching valve (V) are connected in this order in one line; a solvent pump (P2), a switching valve (V), the diffusion promoting device (DU) according to Claim 1, a separation column (C) and a detector (D) are connected in another line; and a switching valve (V), a component

concentration column (M) and a switching valve (V) are connected in a different line[, as shown in Fig. 9].

12. (amended) A method for analyzing a trace amount of a component in a sample with improved detections sensitivity for use in the low flow velocity gradient high performance liquid chromatographic apparatus according to Claim 10, which comprises trapping the target component in the component concentration column (M) by means of a mobile phase discharged from the solvent pump (P1); discharging a different mobile phase from the solvent pump (P2) by turning the switching valve; and eluting the target component from the separation column (C) through diffusion of the target component using the diffusion promoting device (DU) [according to Claim 1 or 3].

13. (amended) A method for analyzing a trace amount of a component in a sample with improved detections sensitivity for use in the low flow velocity gradient high performance liquid chromatographic apparatus according to Claim 11, which comprises injecting the target component into the component concentration column (M) while filling a solvent in the solvent mixer (MC) by means of the solvent pump (P1); discharging a mobile phase from the pump (P2) by turning the switching valve; and eluting the target component from the separation column (C) through diffusion of the target component using the diffusion promoting device (DU) [according to Claim 1 or 3].